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| 10/718,989 | 11/21/2003 | Xuedong Song | KCX-741 (19044) | 9109 |

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| DIRAMIO, JACQUELINE A | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/718,989 | SONG, XUEDONG | |
| | Examiner | Art Unit | |
| | Jacqueline DiRamio | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *64-85 and 89-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64-85 and 89-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

Applicant's amendment to claim 64 is acknowledged, as well as the cancellation of claims 87 and 88.

Currently, claims 64 – 85 and 89 – 92 are pending and under examination.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 64 – 77, 79, 80, and 82 – 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), and in light of O'Riordan et al. ("Monofunctional Derivatives of Coproporphyins for Phosphorescent Labeling of Proteins and Binding Assays," *Anal. Biochem.* **290** (2001) 366-375).

Daniels et al. teach a method for detecting an analyte within a test sample, the method comprising:

i) providing a lateral flow test strip (assay device) that comprises a porous membrane in fluid communication with semiconductor nanocrystals (luminescent or phosphorescent particles) conjugated with a specific binding member, wherein the porous membrane defines a capture region (detection zone) within which is immobilized a capture reagent;

ii) contacting the lateral flow test strip with the test sample;

iii) subjecting the capture region to illumination to generate a detection signal; and

iv) thereafter, measuring the intensity of the detection signal, wherein the amount of the analyte within the test sample is proportional to the intensity of the detection signal (see Figure 1; and paragraphs [0016]-[0028], [0079]-[0082], [0095], [0109], [0111], [0115]-[0120], [0126]-[0128], [0170], and [0212]-[0215]).

However, Daniels et al. fail to teach that the luminescent/phosphorescent particle comprises a phosphorescent label encapsulated within a matrix and that the label has an emission lifetime of about 1 microsecond or more and a Stokes shift of greater than about 100 nanometers.

Klimant teaches of the production and use of luminescent microparticles wherein long-lived phosphorescent labels are incorporated (encapsulated) within solid particles for use as internal standards for referencing phosphorescence signals or as markers for labeling and detecting biomolecules (see column 1, lines 1-16). Luminescence

measurements using phosphorescence signals is a very common method in biological and chemical analysis dues to its high sensitivity and versatility (see column 1, lines 30-35). The incorporation of the phosphorescence labels within matrices allows for elimination or great reduction in phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement (see column 1, lines 17-23).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine with the detection method of Daniels et al. the luminescent microparticles taught by Klimant because Klimant teaches the benefit of luminescent microparticles that comprise phosphorescence labels encapsulated within matrices because the microparticles create long-lived luminescence, wherein the matrices eliminate or greatly reduce phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement.

With respect to Applicant's limitations in claim 64 requiring the phosphorescent labels to have an emission lifetime of about 1 microsecond or more and a Stokes shift of 100 nm or more, the phosphorescent labels used by Klimant preferably comprise metal/ligand complexes that include porphyin complexes of Pt(II) or Pd(II), which are known in the art to have emission lifetimes of 1 microsecond or more and Stokes shift of 100 nm or more (see Klimant: column 3, lines 14-36; and O'Riordan et al.: p366).

With respect to Applicant's claims 65, 66, and 68, Klimant teaches that the phosphorescent label is a metal/ligand complex, particularly comprised of transition metals such as ruthenium, osmium, iridium, rhenium, platinum, or palladium, and also

containing complex ligands, such as **bipyridine**, bipyrazine, phenanthroline, terpyridil or derivatives thereof (see column 3, lines 14-21).

With respect to Applicant's claims 67 and 69, Klimant teaches the phosphorescent label can further comprise a porphyrin ligand or porphyrin complex with platinum(II) or palladium(II), which anticipates Applicant's claims 7 and 31 because the porphyin complexes encompass the derivatives and combinations thereof and are being utilized for the same purpose (see column 3, lines 25-31).

With respect to Applicant's claim 70, Klimant teaches the matrix incorporating the phosphorescent label comprises polymer particles (see column 4, lines 11-19).

With respect to Applicant's claims 71 and 72, Klimant teaches the size of the luminescent particles in the range of 20 µm to 10 µm, particularly from 50 nm to 1 µm (see column 3, lines 37-39).

With respect to Applicant's claim 73, Klimant teaches the matrix incorporating the phosphorescent label protects the label from quenching (see column 1, lines 17-23).

With respect to Applicant's claims 74 and 75, Klimant teaches the matrix incorporating the phosphorescent label protects the label from quenching, enabling the luminescence lifetime (detection signal) to be only 20%, at most 15% and preferably at most 10% shorter than in an $O_2$ free environment, which anticipates Applicant's claims 74 and 75 (see column 3, lines 5-13).

With respect to Applicant's claims 76 and 77, the phosphorescent labels used by Klimant preferably comprise metal/ligand complexes that include porphyin complexes of

Pt(II) or Pd(II), which are known in the art to have emission lifetimes of up to 1000 microseconds (see Klimant: column 3, lines 14-36; and O'Riordan et al.: p366).

With respect to Applicant's claim 79, Daniels et al. teach that the capture reagent in the capture region comprises a specific binding member, such as an antigen, hapten, antibody, or streptavidin (see Figures 1 and 2; and paragraphs [0025], [0088]-[0090], and [0116]).

With respect to Applicant's claim 80, Daniels et al. teach that the illumination source can be a pulsed excitation source (see paragraph [0170]).

With respect to Applicant's claims 82-84, Daniels et al. teach that the specific binding member that is conjugated to the luminescent particles, i.e. semiconductor nanocrystals, is configured to preferentially bind with the analyte and can comprise antigens, haptens, aptamers, and antibodies, as well as analogs of the analyte itself (see paragraphs [0016], [0024], [0088]-[0090], and [0094]-[0098]).

Claims 78 and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), as applied to claim 64 above, and further in view of Zarling et al. (US 5,674,698).

The Daniels et al. and Klimant references, which were discussed in the 103(a) rejection above, fail to teach that the detection signal is measured from 1 to 100 microseconds after the detection zone is subjected to one or more pulses of illumination, or that the signal is measured by a time-gated detector.

Zarling et al. teach of up-converting and down-converting phosphorescent/luminescent reporters for use in biological assays using laser excitation techniques. The detection and quantitation of the phosphorescent reporters is accomplished by illuminating the sample suspected of containing the reporters and detecting the phosphorescent radiation at more or more emission bands. Various means can be used for detection of the phosphorescent emission(s), including a time-gated and/or frequency-gated light detector for rejection of residual background noise. Time-gated detection is desirable because it provides a method of recording long-lived emission after termination of illumination, wherein signal(s) attributable to phosphorescence is recorded, while short-lived autofluorescence and scattered illumination light is rejected. A pulsed excitation source is preferable for use with a time-gated detector, wherein the phosphorescent reporters have emission lifetimes on the order of 1 ms (see Abstract; column 1, lines 12-18; column 31, lines 50-56; column 32, lines 54-67; and column 33, lines 1-18).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al. and Klimant the use of a pulsed excitation source and time-gated detection, wherein the detection signal is measured a certain time period after the excitation as taught by Zarling et al. because Zarling et al. teach the advantages of using a pulsed excitation source and time-gated detection with phosphorescent labels because it provides a method of recording long-lived emission after termination of illumination, wherein

signal(s) attributable to phosphorescence is recorded, while short-lived autofluorescence and scattered illumination light is rejected.

Claims 85 and 89 – 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), as applied to claim 64 above, and further in view of Rylatt et al. (WO 97/009620).

Daniels et al. teach an additional control line or region, but fail to teach that the control line works as a calibration zone, wherein the intensity of the detection signal is calibrated by the intensity of the calibration signal. Klimant also fails to teach the use of a calibration zone.

Rylatt et al. teach a method for quantitative determination of a target analyte in a test sample, comprising a lateral flow assay device wherein a liquid permeable membrane (porous membrane) is used, wherein said membrane contains a test zone (detection zone) and at least one calibration zone(s) (see p4, lines 29-30 and p5, lines 1-20). The membrane also utilizes an analyte detection agent (detection probe) comprising a specific binding partner and an associated label (see p7, lines 25-29 in particular). The test zone (detection zone) utilizes an immobilized analyte receptor (capture reagent) that can bind with the analyte and/or analyte detection agent (detection probe) and generate a detectable signal. The calibration zone includes an immobilized calibration agent receptor that binds to the specific binding partner found on the analyte detection agent (detection probe) or calibration agent (calibration probe) and further, the binding of the agent to the calibration zone produces a calibration signal that

is used to calibrate the signal produced in the test zone (detection signal) (see p5, lines 10-20 and p9, lines 13-19 in particular). Therefore, the lateral flow membrane, containing the analyte detection agent (detection probes), is contacted with the test sample; the analyte detection agent (detection probes) binds to the target analyte and flows to the test zone (detection zone) wherein it binds to an immobilized analyte receptor, and generates a signal, which is detected and measured, thus providing the amount of analyte in the test sample, which is proportional to the intensity of the signal at the test zone (detection signal) calibrated by the intensity of the calibration signal (see p18-20 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al. and Klimant a calibration zone as taught by Rylatt et al. because Rylatt et al. teach the benefit of including a calibration zone with a test zone on a lateral flow assay device in order to provide accurate quantitative determination of a target analyte in a test sample, because the signal produced in the calibration zone is utilized to calibrate the signal produced in the test zone.

Claim 92 is rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220) and Rylatt et al. (WO 97/009620), as applied to claim 85 above, and further in view of Jou et al. (US 5,670,381).

The Daniels et al., Klimant, and Rylatt et al. references discussed above fail to teach that the capture reagent included in the calibration zone comprises a polyelectrolyte.

Jou et al. teach a device for performing an assay comprising a porous material containing a capture or reaction zone with an immobilized capture reagent. The device utilizes a specific binding member attached to a charged substance that is contacted with an analyte of interest to form a complex. The complex binds to the immobilized capture reagent in the capture or reaction zone through ion-capture, wherein the capture reagent is oppositely charged with respect to the charged substance of the analyte complex. The capture reagent preferably comprises an anionic or cationic polymeric substance (polyelectrolyte), which enables the production of a generic solid phase device for use in specific binding assays. Assay procedures for many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test-strip devices. Further, the ion-capture technique increases the potential number of complexes that can be immobilized on the solid support (see column 6, lines 25-40; column 7, lines 1-46; column 10, lines 63-65; column 19, lines 29-67; column 22, lines 29-67; and column 23, lines 1-26).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al., Klimant and Rylatt et al. a polyelectrolyte as the capture reagent in the control region

(calibration zone) as taught by Jou et al. because Jou et al. teach the benefit of using an anionic or cationic polymeric substance as the immobilized capture reagent in a capture zone because the polymeric substance allows for the binding of a conjugated substance or complex to a solid phase support material through ion-capture, which increases the potential number of complexes that can be immobilized on the solid support and allows for the production of a generic solid phase device, wherein many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test-strip devices.

***Response to Arguments***

Applicant's arguments filed October 1, 2007 have been fully considered but they are not persuasive. Applicant argues (see p7-9) that the semiconductor nanocrystals of Daniels et al. do not contain the properties required of Applicant's phosphorescent particles, wherein the particles comprise a phosphorescent label encapsulated within a matrix, and display an emission lifetime of 1 microsecond or more and a Stokes shift greater than about 100 nanometers. Further, Applicant argues that there would be no teaching or motivation to combine the immunochromatographic strip assay of Daniels et al. with the phosphorescent labels of Klimant and O'Riordan et al. in order to arrive at Applicant's claimed invention, particularly because the labels used by the different references would not be considered equivalents and therefore, the only motivation that might exist is one of "obvious to try."

Examiner agrees that the semiconductor nanocrystals of Daniels et al. do not contain the properties required of Applicant's phosphorescent labels, which is why the Daniels et al. reference was combined with Klimant in light of O'Riordan et al. in order to provide a teaching and motivation for substituting the semiconductor labels of Daniels et al. with the phosphorescent labels taught by Klimant, wherein the phosphorescent labels of Klimant do in fact contain the properties required by Applicant's phosphorescent particles. In particular, Klimant teaches the production and use of luminescent microparticles comprising long-lived phosphorescent labels incorporated (encapsulated) within solid particles for use as internal standards for referencing phosphorescence signals or as markers for labeling and detecting biomolecules (see column 1, lines 1-16). Luminescence measurements using phosphorescence signals is a very common method in biological and chemical analysis dues to its high sensitivity and versatility (see column 1, lines 30-35). The incorporation of the phosphorescence labels within matrices allows for elimination or great reduction in phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement (see column 1, lines 17-23). Further, the phosphorescent labels used by Klimant preferably comprise metal/ligand complexes that include porphyin complexes of Pt(II) or Pd(II), which are known in the art to have emission lifetimes of 1 microsecond or more and Stokes shift of 100 nm or more (see Klimant: column 3, lines 14-36; and O'Riordan et al.: p366).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine with the detection method of Daniels et al. the

luminescent microparticles taught by Klimant because Klimant teaches the benefit of luminescent microparticles that comprise phosphorescence labels encapsulated within matrices because the microparticles create long-lived luminescence, wherein the matrices eliminate or greatly reduce phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement.

Applicant's argument that the only motivation to combine the immunochromatographic strip assays of Daniels et al. with the phosphorescent labels of Klimant is one of obvious to try is not found persuasive because, as discussed above, Klimant does provide a teaching and motivation for utilizing the phosphorescent labels as markers in methods of labeling and detecting biomolecules via luminescence, which represents the method taught by Daniels et al. In addition, the semiconductor nanocrystals of Daniels et al., which represent luminescent particles, would be considered functionally equivalent to the luminescent particles of Klimant because both particles provide detectable luminescent/phosphorescent signals when excited by an excitation source, can be conjugated to biomolecules, and can be effectively used as markers for labeling and detecting biomolecules (see paragraphs [0024], [0027], [0028], [0079] and [0082] of Daniels et al.; and column 1, lines 4-16; column 2, lines 51-60; and column 5, lines 23-52 of Klimant).

Finally, there is a reasonable expectation of success to one skilled in the art that the use of the phosphorescent particles taught by Klimant in the immunochromatographic method of Daniels et al. would provide an effective means for labeling and detecting biomolecules via luminescence because Klimant provides

teaching that their phosphorescent labels can be utilized as markers for labeling and detecting biomolecules and there is no suggestion that the use of the phosphorescent particles in the system of Daniels et al. would be inoperative.

***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacqueline DiRamio whose telephone number is 571-272-8785. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jackie DiRamio
Patent Examiner
Art Unit 1641

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